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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/690,115	10/21/2003	Richard L. Apodaca	PRD2033NP	3740
27777	7590	11/14/2006		
PHILIP S. JOHNSON JOHNSON & JOHNSON ONE JOHNSON & JOHNSON PLAZA NEW BRUNSWICK, NJ 08933-7003			EXAMINER COLEMAN, BRENDA LIBBY	
			ART UNIT	PAPER NUMBER
			1624	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/690,115

Applicant(s)

APODACA ET AL.

Examiner

Brenda L. Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-55 is/are pending in the application.
- 4a) Of the above claim(s) 47-50 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-10, 12-20, 31-46 and 51-55 is/are rejected.
- 7) ☒ Claim(s) 11 and 21-30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>8/31/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-4 and 6-55 are pending in the application.

This action is in response to applicants' amendment filed August 31, 2006.

Claims 1, 13, 15, 27, 28, 37 and 38 have been amended.

Response to Amendment

Applicant's amendments filed August 31, 2006 have been fully considered with the following effect:

1. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 42-46 and 54-55 of the last office action labeled paragraph 3, the applicant's arguments have been fully considered, however they were not found persuasive. Claims 44 and 45 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for schizophrenia, does not reasonably provide enablement for all disorders claimed herein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The scope of the method claims are not adequately enabled solely based on the treatment of conditions where to modulation, especially antagonism/inhibition, of the H₃ receptor is beneficial provided in the specification.

In evaluating the enablement question, several factors are to be considered. In *re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5)

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the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the instant invention has claims, which are substituted piperazine compounds.

HOW TO USE: Claims 44-46, 54 and 55 are to a method of treating a variety of psychotic conditions, substance abuse, etc. Any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the effectiveness of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims of the instant invention call for the treatment of any and all diseases associated with the psychosis and substance abuse.

The scope of "treatment of substance abuse" cannot be deemed enabled. The notion that a compound could be effective against chemical dependencies in general is contrary to our current understanding of how chemical dependencies operate. There is not, and probably never will be, a pharmacological treatment for "drug addiction" generally. That is because "drug addiction" is not a single disease or cluster of related disorders, but in fact, a collection with relatively little in common. Addiction to barbiturates, alcohol, cocaine, opiates, amphetamines, benzodiazepines, nicotine, etc all involve different parts of the CNS system; different receptors in the body. For example, cocaine binds at the dopamine re-uptake site. Heroin addiction, for example, arises from binding at the opiate receptors, cigarette addiction from some interaction at

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the nicotinic acid receptors, many tranquilizers involve the benzodiazepine receptor, alcohol involves yet another system, etc. All attempts to find a pharmaceutical to treat chemical addictions generally have thus failed.

Claim 54 calls for the prevention of upper airway allergic response, itch, nasal congestion, or allergic rhinitis, which is not remotely enabled.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo efficacy by those skilled in the art. See *In re Ruskin*, 148 USPQ 221; *Ex parte Jovanovics*, 211 USPQ 907; MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

Claims 44-46, 54 and 55 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for schizophrenia, does not reasonably provide enablement for all disorders claimed herein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for reasons of record and stated above.

2. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 112, second paragraph rejections, labeled paragraph 4a), b), c), d), e), f), g) and h) of the last office action, which are hereby **withdrawn**. However, with regards to the

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35 U.S.C. § 112, second paragraph rejections of claim 44, 45 and 55 labeled paragraph 4i) of the last office action, the applicant's arguments have been fully considered, however they were not found persuasive.

i) The applicants' stated that the physiological role of histamine at the various histamine receptors and the potential therapeutic role of H₃ agonists has been extensively investigated and reported in the literature. The compounds of the invention have been fully described and data suggesting the efficacy of these compounds in treating the claimed disorders has been provided. In view of the broad body of knowledge available to those skilled in the art regarding H₃ agonists and the detailed teachings provided in the specification regarding the claimed compounds, those skilled in the art would be able to determine which disorders could be treated with the claimed compounds and how the claimed compounds should be employed to treat those disorders. The rejection of claims 44, 45 and 55 was on the grounds that it is indefinite, in that it is not known which diseases are capable of being responsive to histamine H₃ receptor activity. The scope of diseases and/or disorders associated with the activity of histamine H₃ receptor could alter over time. The applicants' are not entitled to preempt the efforts of others. Claims 44, 45 and 55 are such that the claim is directed to a method of treatment of a condition mediated by histamine H₃ receptor, thus the applicants have not set forth the metes and bounds of these claims.

Claims 44, 45 and 55 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly

claim the subject matter, which applicant regards as the invention, for reasons of record and stated above.

3. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 102, anticipation rejection of claims 1, 2, 6-10, 21, 42-46 and 51-55, labeled paragraph 5 of the last office action, which is hereby **withdrawn**.

4. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 102, anticipation rejection of claims 1, 2, 6-10, 12-15, 18, 31, 35-38, 42-46 and 51-55, labeled paragraph 6 of the last office action, which is hereby **withdrawn**.

In view of the amendment dated August 31, 2006, the following new grounds of rejection apply:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-4, 6-10, 12-20, 31-46 and 51-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowe et al., U.S. Patent No. 5,883,096. The generic structure of Lowe encompasses the instantly claimed compounds (see Formula (I) column 1) and for the same uses as claimed herein. The examples as set forth in the tables spanning columns 7-30 differ only in the nature of the substituents X, Y, Z, R¹, R², R³, R⁴, R²¹,

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R^{27} , R^{28} and R. Column 1, line 55 through column 6, line 21 defines the substituents X, Y, Z, R^1 , R^2 , R^3 , R^4 , R^{21} , R^{27} , R^{28} and R as follows: one of Y and Z is N and the other is N, CH, or C-alkyl; X is -O-, -S-, -SO-, -SO₂-, -NR⁶-, -CO-, -CH₂-; R is a monocyclic or bicyclic heterocyclic ring as set forth in column 2 and 3; R^1 and R^{21} are independently selected from the group consisting of alkyl, additionally R^1 and R^{21} together may form the group =CH₂, =N-OR⁵, =N-CN, =N-(R⁵)₂, =CH-Alkyl, alkylene, =O, =C(Alkyl)₂, =C(halo)₂.....; R^2 is H, alkyl, alkenyl, cycloalkyl, cycloalkyl substituted with 1 to 3 independently selected R^3 groups, cycloalkenyl, hydroxylC₂-C₂₀alkyl, alkynyl, alkylamide, cycloalkylalkyl, hydroxyarylalkyl, hydroxyarylalkyl, bicycloalkyl, alkynyl, acylaminoalkyl, arylalkyl, hydroxyalkoxyalkyl, azabicyclo, alkylcarbonyl, alkoxyalkyl, aminocarbonylalkyl, alkoxycarbonylaminoalkyl, alkoxycarbonylamino(alkyl)alkyl, alkylcarbonyloxyalkyl, arylhydroxyalkyl, alkylcarbonylamino(alkyl)alkyl, dialkylamino, etc.; R^3 , R^4 , R^{22} , R^{24} , R^{25} are independently selected from the group consisting of H, halo, alkoxy, benzyloxy, benzyloxy substituted by nitro or aminoalkyl, haloalkyl, polyhaloalkyl, nitro, cyano, sulfonyl, hydroxy, amino, alkylamino, formyl, alkylthio, polyhaloalkoxy, acyloxy, trialkylsilyl, alkylsulfonyl, arylsulfonyl, acyl, alkoxycarbonylalkylsulfinyl, -OCONH₂, -OCONH-alkyl, -OCON(alkyl)₂, -NHCOO-alkyl, -NHCO-alkyl, phenyl, hydroxyalkyl, or morpholino; and R^{27} and R^{28} are independently selected from the group consisting of H, alkyl, hydroxyalkyl, arylalkyl, aminoalkyl, haloalkyl, thioalkyl, alkylthioalkyl, carboxyalkyl, imidazolylalkyl, and indolylalkyl, additionally R^{27} and R^{28} may combine to form an alkylene group. The compounds of the instant invention are generically embraced by Lowe in view of the

interchangeability of the substitutions of the piperazine. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R¹ and R²¹ together form an =O as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

Claim Objections

6. Claims 11 and 21-30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Election/Restrictions

7. Claims 47-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 16, 2006.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Brenda L. Coleman
Primary Examiner Art Unit 1624
November 10, 2006